

Medical Risk Management

An educational monograph brought to you by Comprehensive NeuroScience, Inc.



Comprehensive NeuroScience, Inc.

Diabetes in Patients with Schizophrenia

The purpose of this guide is to provide case managers and physicians with information to facilitate treatment of individuals with serious and persistent mental illness who also have co-occurring substance abuse disorder. The guide presents an overview of current research and clinical recommendations for patients with diabetes.

Introduction: Diabetes (also known as Diabetes Mellitus) is a disease in which patients affected cannot regulate their blood sugar. There are two different types of diabetes (see below) that often require different treatments. Patients affected by either of the two types of diabetes are at risk for developing several complications in the future including: blindness, kidney disease, heart disease, stroke, and amputations. A diabetic patient may also be more susceptible to infections, and may be prone to have delayed wound healing. As a result, the care of the diabetic patient by one person becomes an impossible task; it requires a team of health care professionals in order to deliver the best quality care. The case manager plays an integral role in this team assuring the coordination of care.

Compared to everyone else, patients with schizophrenia have increased rates of developing diabetes and cardiovascular disease. No one really knows why that is, but some experts think it may be related to the unhealthy lifestyles of such patients. Such unhealthy lifestyles, along with poor medical follow-up place such patients at an increased risk of experiencing complications from diabetes as well as death. Because of this and other factors, life expectancy for these patients is 57 years for men and 65 years for women, 20% shorter than the general population.

Some medications used recently in the treatment of schizophrenia also place such patients at an increased risk of developing diabetes. The exact mechanism of this is not known and thought to be related to the weight gain associated with these medications; however, there have been reports of schizophrenic patients developing diabetes without having any significant weight gain.

It is important for the case manager to understand that not all schizophrenic patients with diabetes will have been diagnosed and actually know that they have the disease. The purpose of this monogram will be to familiarize the case manager with: (1) the definition of diabetes; (2) risk factors for diabetes, (3) common symptoms of diabetes and screening, (4) management of diabetes, (5) preventing complications of diabetes, and (6) special considerations for patients with schizophrenia.

(1) What is diabetes?

Types of Diabetes: There are two types of diabetes. Type 1 diabetes is usually diagnosed in children and young adults, and was previously known as juvenile diabetes. In type 1 diabetes, the body does not produce any insulin. Insulin is a hormone that helps the body carry sugar from the blood into the cells. Type 2 diabetes is the most common form of diabetes and typically develops in middle age. In type 2 diabetes, either the body does not produce enough insulin or the cells ignore the insulin. Most schizophrenic patients that develop diabetes will develop it during adulthood and thus have type 2 diabetes.

Causes of Diabetes: No one really knows why some people develop diabetes and others do not. It appears that diabetes may be caused by both genetic factors (i.e. it tends to run in families) and environmental factors. The most important environmental factors associated with diabetes are diet and obesity. Several studies have shown that individuals who have a strong family history of diabetes, do not develop diabetes themselves if they maintain a normal weight, proper diet and exercise. In the case of the schizophrenic patient, certain medications may also be associated with the development of diabetes.

Point to Case Manager 1: Schizophrenic patients may be at an increased risk for developing diabetes because of a combination of a family history of diabetes, obesity, poor diet that is high in fat, lack of exercise and some of the medicines they may be taking to treat schizophrenia.

(2) Risk Factors for Diabetes

Patients with schizophrenia are at an increased risk of developing diabetes, whether or not they are on the newer anti-psychotic medications known as “atypical” anti-psychotics. The risk increases further if they are placed on such “atypical” anti-psychotic medications, or if any of the following risk factors are present:

- Weight gain, especially in the central abdominal region
- Family history (first degree relative)
- Ethnicity: African Americans, Hispanic Americans, Asian Americans and Native Americans
- Previous diagnosis of gestational diabetes (diabetes during pregnancy)
- Hypertension, a High Density Lipoprotein (HDL) level below 35 mg/dL, or a triglyceride level above 250 mg/dL are all associated with an increased risk for developing diabetes.

Point to Case Manager 2: Schizophrenic patients should be screened for other risk factors for developing diabetes. If these exist, screening for diabetes should occur early and frequently (i.e. every year) especially if they are on or about to start an atypical anti-psychotic medication.

(3) Common Symptoms of Diabetes and Screening

Some symptoms of diabetes include:

- Frequent urination (also known as polyuria)
- Excessive thirst (also known as polydipsia)

- Extreme hunger
- Unusual weight loss
- Increased fatigue
- Irritability
- Blurry vision

Point to Case Manager 3: The symptoms of diabetes often go ignored because patients, especially schizophrenic patients, do not realize that some of these symptoms may signify a serious health problem. As a result, screening for diabetes becomes very important.

A patient has Diabetes if:

- A random blood sugar greater/or equal to 200 mg/dL is detected, OR
- A fasting blood sugar greater/or equal to 126 mg/dL is detected, OR
- A 2-hour blood sugar greater/or equal to 200 mg/dL is detected after being administered 75 grams of oral sugar. (This is also known as a Glucose Tolerance Test or GTT)

A patient has Impaired Glucose Tolerance (Impaired glucose tolerance can be thought of as “pre-diabetes”) if:

- A 2-hour blood sugar greater/or equal to 140 mg/dL (but less than 200) is detected after being administered 75 grams of oral sugar. (This is also known as a Glucose Tolerance Test or GTT), OR
- A fasting blood sugar between the ranges of 110 to 125.

Because of the fact that patients with schizophrenia are at an increased risk for developing diabetes overall, the risk further increases if they get started on an atypical anti-psychotic medication and because of the fact that if they do develop diabetes, schizophrenic patients tend to have worse outcomes, it is recommended that every schizophrenic patient:

- 1) Have a risk assessment done inquiring about family history, ethnicity, diet and exercise.
- 2) Measure the body mass index (BMI), blood pressure, and cholesterol panel
- 3) Screen for diabetes with a fasting blood glucose early and frequently (early= for all schizophrenic patients, regardless of age; frequently= at least once a year)

(4) Management of Diabetes

Diabetes can be managed successfully by eating well, exercising, and managing stress.

The principles of management include:

- Faithful monitoring of blood sugars, especially when ill (such as when someone has an infection), or when stressed.
- Glucose before meals should be between 80-120 mg/dL and two hours after meals between 100-140 mg/dL
- Check urine for ketones when blood sugar is 250 mg/dl or higher. Ketones are breakdown products of the body. They should **never** be present in the

urine. If they are present in the urine, it signifies the fact that this person's blood sugars are going out of control and thus, the patient should seek immediate medical attention.

- It is important to pay attention to meal plan balance and timing. Patients should see a nutritionist at least initially.
- Stress management
- Regular exercise program
- Medications when needed (including insulin)

Hemoglobin A1c (a blood test) can determine the average amount of sugar the body has been exposed to over the past three months. The results are measured in a percentage. The usual lab reference range for a normal HgbA1c is from 4.4 - 6.4 percent. If the number is eight percent or above, the risk for diabetes complications increases.

Point to Case Manager 4: Every schizophrenic patient with Diabetes should have a hemoglobin A1c level (also known as HbA1c or glycosylated Hemoglobin) checked at least twice a year. If this level is above eight percent, the patient is NOT in optimal control.

Medications: The following is a list of medications commonly used to regulate blood glucose in diabetics.

Types of medications

Drug family	Brand name	Generic name
Sulfonylureas		
	Amaryl	Glimepiride
	Diabeta	Glyburide
	Glucotrol XL	Glipizide
	Glynase	Micronized Glyburide
Biguanides		
	Glucophage	Metformin
Thiazolidinedione		
	Avandia	Rosiglitazone
	Actos	Pioglitazone
Alpha-glucosidase inhibitors		
	Precose	Acarbose
	Glyset	Miglitol
Meglitinides		
	Prandin	Repaglinide
	Starlix	Nateglinide
Combination oral agents		

Glucovance	Glyburide + Metformin
Avandamet	Rosiglitazone + Metformin

Type I diabetes can only be managed with insulin therapy. Type II diabetes is often managed with the oral agents outlined above, but sometimes insulin must also be added to obtain maximum control.

Point to Case Manager 5: If patients are started on a Thiazolidinedione, they need to have their liver function checked (via a liver profile blood test) frequently to assure that this medication is not causing any liver problems.

Point to Case Manager 6: If patients are started on Glucophage (Metformin), they need to have their kidney function checked (blood creatinine level). In patients with kidney disease, this medication may stay in the body longer and subsequently accumulate to toxic levels.

Point to Case Manager 7: Patients started on the Sulfonylurias need to be monitored for hypoglycemia (low blood glucose). Out of all the medications in the table above, only the Sulfonylurias can cause hypoglycemia.

Patients with impaired glucose tolerance (pre-diabetes) usually do not require any medications. In these patients a diet should be prescribed, along with exercise and they should be followed very closely for the possibility of developing diabetes in the future.

It is important to note that managing blood sugars with either diet/exercise, medications or insulin, is only one part of managing diabetes. An equally important part of managing this disease involves screening (and if possible preventing) complications of the disease from occurring. The next section focuses on this.

(5) Preventing complications of diabetes

Diabetes can be associated with both short-term and long-term complications.

Short-term complications: A condition known as Diabetic ketoacidosis, or DKA is a life-threatening complication most often associated with type 1 diabetes, however, it is also occurring more frequently in patients with type 2 diabetes, which is the most common form seen in the schizophrenic population. This is of significant concern since 6-10% of DKA patients may die if it is not identified and treated early. The mortality rate of DKA may be even higher in schizophrenia since these patients may not be as vigilant as the general public in seeking medical treatment for illness. DKA occurs when a person's blood sugar goes up very high (usually above 500, but at times can go as high as over 1000). As a result of these high blood sugars, acids build up in the patient's blood and the condition known as DKA occurs. The main causes of DKA include underlying or concomitant infection (40%, most often are urinary tract infections or pneumonia), missed insulin treatments (25%), and newly diagnosed, previously unknown diabetes (15%). DKA occurs when there is a state of insulin deficiency aggravated by elevated intermediary blood sugars, dehydration, and acid-producing elements in the blood.

Patients who may be developing DKA will complain of fatigue, malaise, thirst, and frequent urination. Depending on the length of symptoms the patient may be able to report weight loss. As the patient becomes increasingly ill they may begin to vomit and complain of abdominal pain and have a fruity smelling breath.

If you suspect that a patient may be developing DKA, urgent treatment is required. The treatment goals of the patient with DKA are as follows: (1) improve the dehydration with intra-venous fluids, (2) decrease the serum sugar (emergent inpatient insulin treatment), (3) reverse the acidic state in the patient's blood, (4) correct electrolyte losses and imbalances, and (5) find and treat the underlying causes.

Point to Case Manager 8: Any schizophrenic patient suspected of having DKA should be immediately referred to EMERGENT medical attention.

Other short-term complications include the fact that diabetics are more susceptible to infections and if injured take longer to heal when compared to the general population.

Point to Case Manager 9: Every diabetic patient should be offered the pneumonia vaccine every six years and the flu vaccine every year because of the fact that they are more susceptible to these infections.

Long-term complications:

The long-term health problems that occur in diabetes are caused by injury to both large and small blood vessels. Over time micro-vascular (small blood vessel) disease damages the kidneys, peripheral nerves and retina (vision). This can also lead to erectile dysfunction (impotence) and gastroparesis (constipation, bowel obstruction). Macro-vascular disease increases the risk of hypertension, stroke and heart attacks seen in patients with type 2 diabetes. (See cardio-vascular disease monogram for more information)

Screening for kidney disease: Every patient should have a blood creatinine test and a urine micro-albumin test done once a year. The blood creatinine test measures kidney function, but by the time an abnormality is picked up by this blood test, a significant amount of the kidneys may already be damaged. For this reason, a urine micro-albumin test is required. This urine test is able to detect early damage to the kidneys from diabetes. Anyone who has positive micro-albumin in the urine, should be started on Ace-inhibitor medications. Such medications have been shown to slow down the progression of kidney disease in the diabetic.

Screening for peripheral nerve damage: Diabetes is one of the leading causes of leg/feet amputations, partly because of peripheral nerve damage resulting in decreased sensation to the legs and feet. As a result, these patients are more prone to injure their legs and feet and not feel anything. Any patient with diabetes should have at least an annual foot exam to determine both sensory perception and circulation to the legs and feet. If there is damage to the nerves and/or circulation to the legs and feet, diabetics should be instructed on proper foot care.

Screening for diabetic retinopathy: Diabetes is the leading cause of blindness in this country. Because there are no symptoms or loss of vision until there is significant damage already present, yearly diabetic eye exams are necessary to detect early damage (microscopic hemorrhages) or changes to the eye. Damage to the retina can be prevented with good blood sugar management.

Screening for macro-vascular disease: In terms of preventing macro-vascular complications from occurring in the diabetic patient, the most important thing to do is to screen for high blood pressure and elevated lipids (cholesterol). Ninety-seven percent of the people with diabetes have abnormal cholesterol levels. Therefore, fasting lipid levels should be included as part of annual blood evaluations. The standard of treatment is to maintain the Low-Density Lipoproteins (LDL) levels below 100 in every diabetic. Recent evidence now suggests that all diabetics should be started on cholesterol-reducing medications (regardless of their cholesterol levels) in order to decrease the risk of developing heart disease. Finally, tight control of blood pressure is also essential in the diabetic. Elevated blood pressure places a diabetic at risk for developing both macro-vascular and micro-vascular disease.

(6) Special considerations for patients with schizophrenia.

There are a growing number of reports suggesting an association of treatment with some atypical anti-psychotic medications and weight gain, new onset of type 2 diabetes, exacerbation of existing diabetes, and in rare instances death. The onset or exacerbation of diabetes with these agents occurred even in those patients who were not obese. Examination of all the available data consistently shows that patients treated with clozapine or olanzapine have an increased risk for diabetes compared to patients treated with other atypical anti-psychotics. The risk associated with risperidone and quetiapine was less clear. For aripiprazole and ziprasidone there does not appear to be increased risk.

Point to Case Manager 10: A schizophrenic patient being started on clozapine or olanzapine needs to be carefully monitored for the onset of diabetes, exacerbation of existing diabetes, or the onset of DKA. This can occur even in those patients who do not experience weight gain and are not obese. The risk associated with risperidone and quetiapine is less clear.

In healthy, non-diabetic patients, the following assessments should be performed **before** starting treatment with an atypical anti-psychotic medication:

- Height and weight
- Body mass index (BMI)
- Waist circumference
- Fasting plasma glucose and lipid levels

The frequency with which laboratory measures are repeated will vary considerably based on clinical history but should be repeated at least once a year. Obtaining baseline values

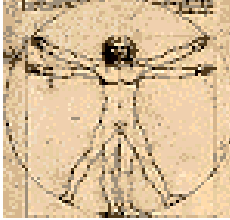
of the relevant physical and laboratory parameters including blood pressure, weight, height, BMI, waist circumference, fasting serum lipids (total, LDL, and HDL cholesterol along with triglycerides), and a fasting plasma glucose level is critical prior to initiating anti-psychotic medications. During the initiation of anti-psychotic treatment, patients should have these values monitored regularly, although frequency must be dictated by the individual patient's level of risk. For example, an obese schizophrenia patient with a family history of diabetes who has gained 30 pounds on his current anti-psychotic medication demands more intensive monitoring than a slender patient with no family history of diabetes who is not gaining weight during anti-psychotic treatment. In general, assessments should be made more frequently during the initial titration phase of treatment. Nevertheless, all schizophrenia patients treated with anti-psychotic medication should have a yearly assessment of fasting lipids and glucose. The Consensus Development Conference recommends monitoring of weight every 4 weeks for the first 3 months and then quarterly thereafter. Blood pressure and fasting glucose should be measured after 3 months and then annually. Fasting lipids are recommended to be measured after 3 months and then every 5 years. Similarly, vital signs, weight, and waist circumference should be measured at every visit, as these are simple measures to monitor that have a high yield of alerting clinicians to adverse metabolic side effects of anti-psychotic medications.

Point to Case Manager 11: The risk of diabetes can be managed effectively by (1) consideration of metabolic risks when starting atypical anti-psychotics, (2) patient, family, and care giver education, (3) baseline screening, (4) regular monitoring, and (5) referral to specialized services when appropriate.

When treatment-emergent weight gain, elevations in cholesterol profile, and/or diabetes are observed, switching to another agent that is not associated with significant weight gain or diabetes should be considered. For certain situations clinical benefits may outweigh risks, as is the case with clozapine (improvement in treatment refractory patients outweighs risk of metabolic side effects). These patients should also be referred to diabetes self-management education programs as well as a specialist for further medical consultation.

Finally, case managers and clinicians need to be aware of the signs and symptoms of acute metabolic deterioration (e.g., DKA). Confusion, abdominal pain, nausea, frequent urination and thirst can be indicative of life threatening complications and these symptoms should prompt emergent evaluation and treatment.

In addition, schizophrenia patients suffer from impaired insight, lack of resources (i.e., access to medical care), lower medication and treatment compliance, and more psychosocial stress, all of which can compound medical problems. For these reasons, the case manager must at times be pro-active in terms of assessing the patient for any of the above noted symptoms.



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Points to Case Managers:

1. The following risk factors place a schizophrenic patient at increased risk of developing diabetes: obesity, sedentary lifestyle, family history, ethnicity, elevated blood pressure, abnormal lipid profile, gestational diabetes (diabetes during pregnancy).
2. Certain atypical anti-psychotic medications have been associated with diabetes; these have included: clozapine and olanzapine. This can occur even in those patients who do not experience weight gain and are not obese. The risk associated with risperidone and quetiapine is less clear.
3. Common symptoms of Diabetes include: frequent urination (also known as polyuria), excessive thirst (also known as polydipsia), extreme hunger, unusual weight loss, increased fatigue, irritability, blurry vision.
4. A patient has Diabetes if: A random blood sugar greater/or equal to 200 mg/dL is detected, OR a fasting blood sugar greater/or equal to 126 mg/dL is detected, OR a 2-hour blood sugar greater/or equal to 200 mg/dL is detected after being administered 75 grams of oral sugar. (This is also known as a Glucose Tolerance Test or GTT).
5. Every schizophrenic patient should have a hemoglobin A1c level checked at least twice a year. If this level is above eight percent, the patient is NOT in optimal control.
6. If patients are started on a Thiazolidinedione, they need to have their liver function checked frequently to assure that this medication is not causing any liver problems.
7. If patients are started on Glucophage (Metformin), they need to have their kidney function checked (blood creatinine level). In patients with kidney disease, this medication may stay in the body longer and subsequently accumulate to toxic levels.
8. Patients started on the Sulfonylurias need to be monitored for hypoglycemia (low blood glucose).

- 9. Symptoms of DKA include: fatigue, malaise, thirst, and frequent urination, vomit, abdominal pain and a fruity smelling breath or breath that smells like alcohol. Any schizophrenic patient suspected of having DKA should be immediately referred to EMERGENT medical attention.**
- 10. Every diabetic patient should be offered the pneumonia vaccine every six years and the flu vaccine every year because of the fact that they are more susceptible to these infections.**
- 11. A urine micro-albumin test is required every year. This urine test is able to detect early damage to the kidneys from diabetes. Anyone who has positive micro-albumin in the urine should be started on Ace-inhibitor medications. Such medications have been shown to slow down the progression of kidney disease in the diabetic.**
- 12. Any patient with diabetes should have at least an annual foot exam to determine both sensory perception and circulation to the legs and feet. If there is damage to the nerves and/or circulation to the legs and feet, diabetics should be instructed on proper foot care.**
- 13. Yearly diabetic eye exams are necessary to detect early damage (microscopic hemorrhages) or changes to the eye.**
- 14. The standard of treatment is to maintain the Low-Density Lipoproteins (LDL) levels below 100 in every diabetic. Recent evidence now suggests that all diabetics should be started on cholesterol-reducing medications (regardless of their cholesterol levels) in order to decrease the risk of developing heart disease.**
- 15. Tight control of blood pressure is also essential in the diabetic. Elevated blood pressure places a diabetic at risk for developing both macro-vascular and micro-vascular disease.**